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EXAMINER	
CROW, ROBERT THOMAS	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/821,239	JOYCE, TIMOTHY H.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) *21-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 30-53* is/are rejected.

7)☒ Claim(s) *33,35, and 40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ;
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I in the reply filed on 26 May 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 21-29 are withdrawn. Claims 1-20 and 30-53 are under prosecution.

Claim Objections

1. Claims 33 and 40 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 33 and 40 each dependent upon themselves, and therefore do not further limit the subject matter of a previous claim. For examination purposes, claim 33 is interpreted as being dependent upon claim 30, and claim 40 is interpreted as being dependent upon claim 37.

2. Claim 35 is objected to because of the following informalities: Claim 35 recites "a tranlocating chemical moiety" in line 12 of the claim. This appears to be a typographical error. Appropriate correction is required.

Claim Rejections - 35 USC § 112 Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20, 31-33 36, 38, 39, 40, 41, 46, 47, 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claims 1-20 are indefinite in claim 1, which recites the limitation "the second ring electrode" in lines 11-12 of the claim. There is insufficient antecedent basis for "the second ring electrode" in "the second ring adjacent to the first ring electrode" in line 10 of the claim. It is suggested that the claim be amended to reflect proper antecedent basis.

2. Claim 4 is indefinite in the recitation "a second substrate for positioning the second substrate" at the end of the claim. It is unclear how a second substrate is used for positioning itself.

3. Claims 9-12 are each in definite in the recitation "the probe" in line 1 of each of the claims. There is insufficient antecedent basis for these limitations in the apparatus of claim 1. It is suggested that "the probe" be changed to "a probe of the array."

4. Claim 14 is indefinite in the recitation "the micro fluidic channel" in line 1 of the claim. There is insufficient antecedent basis for "the micro fluidic channel" in "a channel" in line 3 of claim 1. It is suggested the phrase "micro fluidic" be deleted from the claim.

5. Claims 31-33 are indefinite.

   A. Claim 33 is rejected because it depends upon itself.

   B. Claims 31-32 each depend upon claim 33, and are therefore rejected as being dependent upon a claim that is dependent upon itself.

It is suggested that claims 31-33 be amended to reflect proper dependency. It is also suggested that the amendments to the claims be carefully checked for proper antecedent basis.

6. Claims 36, 38, 39, and 40 are indefinite.

   A. Claim 36 is rejected because it depends upon itself.

   B. Claim 36 is also indefinite in the recitation "the biopolymer" in line 1 of the claim. There is insufficient antecedent basis for "the biopolymer" in "a chemical moiety" in claim 35. It is suggested that the claim be amended to reflect proper antecedent basis.

   C. Claims 38 and 39 are each rejected because each claim depends upon claim 40, and are therefore rejected as being dependent upon a claim that is dependent upon itself.

D. Claim 39 is also indefinite in the recitation "the first diameter portion of the nanopore being smaller than the second diameter portion of the nanopore" in the last two lines of the claim. Claim 37 already defines the first insulator edge as overhanging the first electrode edge; therefore, it is unclear how claim 37 further limits the diameters of the nanopore.

E. Claim 36 rejected because it depends upon claim 38, and is therefore rejected as being dependent upon a claim that is dependent upon a claim that is dependent upon itself.

It is suggested that claims 36, 38, and 40 be amended to reflect proper dependency. It is also suggested that the amendments to the claims be carefully checked for proper antecedent basis.

7. Claim 41 is indefinite in the recitation "the second insulator edge" in line 1 of the claim. Because the claim dependency is improper under 37 CFR 1.75(c), the antecedent basis for "the second insulator edge" is unclear. It is suggested the claim be amended for proper dependency and carefully checked for proper antecedent basis.

8. Claim 46 is indefinite in the recitation "the electric circuit" in line 1 of the claim. Because the claim dependency is improper under 37 CFR 1.75(c), the antecedent basis for "the electric circuit" is unclear. It is suggested the claim be amended for proper dependency and carefully checked for proper antecedent basis.

9. Claim 47 is indefinite in the recitation "the voltage source" in line 1 of the claim. Because the claim dependency is improper under 37 CFR 1.75(c), the antecedent basis for "the voltage source" is unclear. It is suggested the claim be amended for proper dependency and carefully checked for proper antecedent basis.

10. Claim 48 is indefinite in the recitation "the electric circuit" in line 1 of the claim. Because the claim dependency is improper under 37 CFR 1.75(c), the antecedent basis for "the electric circuit" is

unclear. It is suggested the claim be amended for proper dependency and carefully checked for proper antecedent basis.

Claim Rejections - 35 USC § 112 Sixth Paragraph

The following is a quotation of the sixth paragraph of 35 U.S.C. 112:

> An element in a claim for a combination may be expressed as a means or step for performing a specified function without the recital of structure, material, or acts in support thereof, and such claim shall be construed to cover the corresponding structure, material, or acts described in the specification and equivalents thereof.

The limitations "a means for signal detection" in line 1 of claim 6 and "means to move the fluids" in line 1 of claim 20 are not being treated under 35 USC 112, sixth paragraph because the Specification does not provide explicit limitations as to the means for providing the various functions found in the claims.

Claim Interpretation

It is noted that claim 31-32, 36, 38-39, 41, and 46-48 depend from higher numbered claims. While theses may bi typographical errors, the claims are examined as detailed below.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8, 13-14, 17-18, 20, 30-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al (U.S. Patent Application Publication No. US 2002/0182627 A1, published 5 December 2002).

Regarding claim 1, Wang et al teach an apparatus for identifying a chemical moiety from a sample solution, comprising:

a substrate having a channel (e.g., a microfluidic device having a channel; paragraphs 0062 and 0408 and Figures 13 and 21) with at least one array for capturing and releasing a chemical moiety from a sample solution (e.g., a proteomics unit or genomics unit; paragraphs 0411-412); and

a solid state nanopore system downstream from the substrate (Figure 21, wherein the first chamber is a proteomics or genomics unit [i.e., any appropriate test takes place in the first chamber], and the sample is transported from the first chamber to an ion transport detection unit; paragraph 0408) for identifying the chemical moiety received from the substrate channels after the chemical moiety has been released from the array (e.g., the ion transport detection unit receives the samples from the first chamber; paragraph 0408 and Figure 21), the nanopore system comprising:

a first ring electrode (e.g., a spiral electrode structure [paragraph 0038 and Figure 3B], wherein the electrodes are circular; paragraph 0128);

a second ring adjacent to the first ring electrode (e.g., the second electrode 61 of Figure 10 (paragraph 0059], wherein the electrodes are circular [i.e., rings]; paragraph 0128);

a nanopore adjacent to the first ring electrode and the second ring electrode and positioned to allow the chemical moiety to be positions in the first ring electrode and the second ring electrode (i.e., hole 12 of Figure 10; paragraph 0059); and

a voltage source for electrically connecting the first ring electrode to the second ring electrode for applying a ramping potential from the first ring electrode, through a portion of the chemical moiety in the nanopore to a second ring electrode to produce a signal indicative of a portion of the chemical moiety (e.g., the electrodes measure ion transport across the hole [paragraph 0341], wherein a feedback capacitor ramps a voltage [paragraph 0345], and the electrical measurements are detected; paragraph 0342).

Regarding claim 2, Wang et al teach the apparatus of claim 1, further comprising a substrate for positioning the first electrode and the second electrode (e.g., the electrodes are provided on a separate

layer [paragraph 0186], wherein the layer is interpreted as a substrate for these additional structures, and wherein the layer is formed by dipping the substrate of claim 1 [paragraph 0191]; therefore, the layer is a single substrate formed on the substrate of claim 1).

Regarding claim 3, Wang et al teach the apparatus of claim 1, further comprising at least a first substrate for positioning the first electrode (e.g., the electrodes are provided on separate layers [paragraph 0186], wherein each layer is interpreted as a substrate for these additional structures).

Regarding claim 4, Wang et al teach the apparatus of claim 1, further comprising at least a second substrate for positioning the second substrate (e.g., the electrodes are provided on separate layers [paragraph 0186], wherein each layer is interpreted as a substrate for these additional structures).

Regarding claim 5, Wang et al teach the apparatus of claim 1, further comprising at least a first substrate for positioning a nanopore (e.g., Figure 9, wherein hole is in the substrate; paragraph 0058).

Regarding claim 6, Wang et al teach the apparatus of claim 1, further comprising a means for signal detection for detecting the signal produced from the portion of the biopolymer (e.g., the ion transport detection unit; paragraph 0408).

Regarding claim 7, Wang et al teach the apparatus of claim 1, wherein the channel is a microfluidic channel (paragraph 0080).

Regarding claim 8, Wang et al teach the apparatus of claim 1, wherein the array comprises a probe (e.g., the array is a genomics unit that includes structures [i.e., probes] for ex vivo hybridization to nucleic acids; paragraph 0412).

Regarding claim 13, Wang et al teach the apparatus of claim 1, wherein the substrate comprises glass (paragraph 0026).

Regarding claim 14, Wang et al teach the apparatus of claim 2, wherein the dimension of the micro fluidic channel is 100 microns or less (e.g., the channels [i.e., conduits] are 10 microns; paragraph 0114).

Regarding claim 17, Wang et al teach the apparatus of claim 1, wherein the substrate is rigid (e.g., glass; paragraph 0026).

Regarding claim 18, Wang et al teach the apparatus of claim 1, which further comprises valves in the channel that permit different fluids to be directed into the channel (paragraph 0402).

Regarding claim 20, Wang et al teach the apparatus of claim 1, which further comprises means to move the fluids through the array (e.g., the chambers are fed by pumps; paragraph 0195).

Regarding claim 30, Wang et al teach an apparatus for identifying a chemical moiety from a sample solution, comprising:

a substrate having a channel (e.g., a microfluidic device having a channel; paragraphs 0062 and 0408 and Figures 13 and 21) with at least one array for capturing a chemical moiety from a sample solution (e.g., a proteomics unit or genomics unit; paragraphs 0411-412); and

a solid state nanopore system downstream from the substrate (Figure 21, wherein the first chamber is a proteomics or genomics unit [i.e., any appropriate test takes place in the first chamber], and the sample is transported from the first chamber to an ion transport detection unit; paragraph 0408) for identifying the chemical moiety received from the substrate channels after the chemical moiety has been released from the array (e.g., the ion transport detection unit receives the samples from the first chamber; paragraph 0408 and Figure 21), the nanopore system comprising:

a first electrode having a first nanopore (e.g., a spiral electrode structure surrounding a hole in the substrate [paragraph 0038 and Figure 3B], wherein the electrodes are circular; paragraph 0128);

a second electrode adjacent to the first electrode (e.g., the second electrode 61 of Figure 10; paragraph 0059) having a second nanopore (e.g., the electrodes are circular [i.e., rings; paragraph 0128] and surrounds the bottom of the hole in the substrate; Figure 10) wherein the first nanopore of the first electrode is positioned with the second nanopore of the second electrode so that the chemical moiety may translocate through the first nanopore and the second nanopore (e.g., the hole that is surrounded by the electrodes is used as an ion transport channel; paragraph 0077); and

a voltage source for electrically connecting the first electrode to the second electrode for applying a ramping potential from the first electrode, through a portion of the chemical moiety in the nanopore to a second electrode to produce a signal indicative of a portion of the chemical moiety (e.g., the electrodes measure ion transport across the hole [paragraph 0341], wherein a feedback capacitor ramps a voltage [paragraph 0345], and the electrical measurements are detected; paragraph 0342).

Regarding claim 31, Wang et al teach the apparatus of claim 30, wherein the first and second nanopores have center points and wherein the center point of the first nanopore is positioned coaxially with the center point of the second electrode (e.g., the hole [i.e., in the substrates] is at the center of the spiral electrode elements; paragraph 0239).

Regarding claim 32, Wang et al teach the apparatus of claim 30, wherein the first electrode is positioned above the second electrode (e.g., electrode 60 is above electrode 61 of Figure 10).

Regarding claim 33, Wang et al teach the apparatus of claim 30, further comprising a substrate for positioning the first electrode and the second electrode (e.g., the electrodes are provided on a separate layer [paragraph 0186], wherein the layer is interpreted as a substrate for these additional structures, and wherein the layer is formed by dipping the substrate of claim 1 [paragraph 0191]; therefore, the layer is a single substrate formed on the substrate of claim 1).

Regarding claim 34, Wang et al teach the apparatus of claim 33, further comprising at least a second substrate for positioning the second electrode (e.g., the electrodes are provided on separate layers [paragraph 0186; i.e., the dipped substrate of claim 33 has an additional layer for the second electrode; paragraph 0186], wherein each layer is interpreted as a substrate for these additional structures).

Regarding claim 35, Wang et al teach an apparatus for identifying a chemical moiety from a sample solution, comprising:

a substrate having a channel (e.g., a microfluidic device having a channel; paragraphs 0062 and 0408 and Figures 13 and 21) with at least one array for capturing a chemical moiety from a sample solution (e.g., a proteomics unit or genomics unit; paragraphs 0411-412); and

a solid state nanopore system downstream from the substrate (Figure 21, wherein the first chamber is a proteomics or genomics unit [i.e., any appropriate test takes place in the first chamber], and the sample is transported from the first chamber to an ion transport detection unit; paragraph 0408) for identifying the chemical moiety received from the substrate channels after the chemical moiety has been released from the array (e.g., the ion transport detection unit receives the samples from the first chamber; paragraph 0408 and Figure 21), the nanopore system comprising:

a first electrode (e.g., a spiral electrode structure surrounding a hole in the substrate [paragraph 0038 and Figure 3B], wherein the electrodes are circular; paragraph 0128);

a second electrode spaced from the first electrode to define a nanopore between the first electrode and the second electrode (e.g., the second electrode 61 of Figure 10 [paragraph 0059]; wherein the electrodes are circular [i.e., rings; paragraph 0128] and surround the bottom of the hole in the substrate [Figure 10], thereby defining the nanopore), the nanopore designed for receiving a translocating chemical moiety (e.g., the hole that is surrounded by the electrodes is used as an ion transport channel; paragraph 0077), the first electrode being in electrical connection with the second electrode (e.g., electrical connection leads from the electrodes connect to a measuring device; paragraph 0058); and

a voltage source for electrically connecting the first electrode to the second electrode for applying a ramping potential from the first electrode, through a portion of the chemical moiety in the nanopore to a second electrode to produce a signal indicative of a portion of the chemical moiety (e.g., the electrodes measure ion transport across the hole [paragraph 0341], wherein a feedback capacitor ramps a voltage [paragraph 0345], and the electrical measurements are detected; paragraph 0342).

Regarding claim 36, Wang et al teach the apparatus of claim 35, wherein the biopolymer is translocated in a stepwise fashion through the nanopore defined between the first electrode and the second electrode (e.g., Figure 7, wherein a particle first engages the hole [paragraph 0053], then is moved into the hole; paragraph 0054).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1, 9, 15, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (U.S. Patent Application Publication No. US 2002/0182627 A1, published 5 December 2002) in view of Yasuda et al (U.S. Patent No. 6,218,126 B1, issued 17 April 2001).

Regarding claim 9, Wang et al teach the apparatus of claim 1 for identifying a chemical moiety from a sample solution, comprising:

A substrate having a channel (e.g., a microfluidic device having a channel; paragraphs 0062 and 0408 and Figures 13 and 21) with at least one array for capturing and releasing a chemical moiety from a sample solution (e.g., a proteomics unit or genomics unit; paragraphs 0411-412); and

a solid state nanopore system downstream from the substrate (Figure 21, wherein the first chamber is a proteomics or genomics unit [i.e., any appropriate test takes place in the first chamber], and the sample is transported from the first chamber to an ion transport detection unit; paragraph 0408) for identifying the chemical moiety received from the substrate channels after the chemical moiety has been released from the array (e.g., the ion transport detection unit receives the samples from the first chamber; paragraph 0408 and Figure 21), the nanopore system comprising:

a first ring electrode (e.g., a spiral electrode structure [paragraph 0038 and Figure 3B], wherein the electrodes are circular; paragraph 0128);

a second ring adjacent to the first ring electrode (e.g., the second electrode 61 of Figure 10 (paragraph 0059], wherein the electrodes are circular [i.e., rings]; paragraph 0128);

a nanopore adjacent to the first ring electrode and the second ring electrode and positioned to allow the chemical moiety to be positions in the first ring electrode and the second ring electrode (i.e., hole 12 of Figure 10; paragraph 0059); and

a voltage source for electrically connecting the first ring electrode to the second ring electrode for applying a ramping potential from the first ring electrode, through a portion of the chemical moiety in the nanopore to a second ring electrode to produce a signal indicative of a portion of the chemical moiety (e.g., the electrodes measure ion transport across the hole [paragraph 0341], wherein a feedback capacitor ramps a voltage [paragraph 0345], and the electrical measurements are detected; paragraph 0342).

While Wang et al teach an array having probes (e.g., the array is a genomics unit that includes structures [i.e., probes] for ex vivo hybridization to nucleic acids; paragraph 0412), Wang et al do not explicitly teach the probes are nucleic acids.

However, Yasuda et al teach an apparatus (Title) comprising an array of complementary polynucleotide probes (i.e., nucleic acid probes) immobilized on a substrate (Abstract and Figure 3) with the added advantage that polynucleotide probes allows selective extraction of a target polynucleotide alone from a sample solution (column 2, lines 25-27).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the apparatus comprising the probe array as taught by Wang et al with the nucleic acid probes as taught by Yasuda et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in selective extraction of a target polynucleotide alone from a sample solution as explicitly taught by Yasuda et al (column 2, lines 25-27).

Regarding claim 15, the apparatus of claim 1 is discussed above. While Wang et al teach preferred targets are biomolecules (paragraph 0429), Wang is silent with respect to oligonucleotides being targets.

However, Yasuda et al teach an apparatus (Title) comprising an array immobilized on a substrate (Abstract and Figure 3) having oligonucleotides (e.g., mRNA) as targets with the added advantage that polynucleotide (i.e., mRNA) targets are quantitatively determined to allow clarification of a condition in a white blood cell (column 21, lines 33-41).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the apparatus comprising the probe array as taught by Wang et al with the oligonucleotide targets as taught by Yasuda et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in quantitative determination of the polynucleotide targets to allow clarification of a condition in a white blood cell as explicitly taught by Yasuda et al (column 21, lines 33-41).

Regarding claim 19, the apparatus of claim 1 is discussed above. Wang et al are silent with respect to temperature control.

However, Yasuda et al teach an apparatus (Title) comprising an array of complementary polynucleotide probes.(i.e., nucleic acid probes) immobilized on a substrate (Abstract and Figure 3) and further comprising a temperature control device (e.g., an infrared laser source; column 6, lines 4-35) with the added advantage that the temperature control device (i.e., the infrared laser) allows selective separation of a hybridized target polynucleotide from a probe on a specific area (column 6, lines 30-35).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the apparatus as taught by Wang et al with the temperature control device as taught by Yasuda et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in allowing selective separation of a hybridized target polynucleotide from a probe on a specific area as explicitly taught by Yasuda et al (column 6, lines 30-35).

2. Claims 1, 10, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (U.S. Patent Application Publication No. US 2002/0182627 A1, published 5 December 2002) in view of Chin et al (U.S. Patent No 6,197,599 B1, issued 6 March 2001).

Regarding claim 10, Wang et al teach the apparatus of claim 1 for identifying a chemical moiety from a sample solution, comprising:

A substrate having a channel (e.g., a microfluidic device having a channel; paragraphs 0062 and 0408 and Figures 13 and 21) with at least one array for capturing and releasing a chemical moiety from a sample solution (e.g., a proteomics unit or genomics unit; paragraphs 0411-412); and

a solid state nanopore system downstream from the substrate (Figure 21, wherein the first chamber is a proteomics or genomics unit [i.e., any appropriate test takes place in the first chamber], and the sample is transported from the first chamber to an ion transport detection unit; paragraph 0408) for identifying the chemical moiety received from the substrate channels after the chemical moiety has been released from the array (e.g., the ion transport detection unit receives the samples from the first chamber; paragraph 0408 and Figure 21), the nanopore system comprising:

a first ring electrode (e.g., a spiral electrode structure [paragraph 0038 and Figure 3B], wherein the electrodes are circular; paragraph 0128);

a second ring adjacent to the first ring electrode (e.g., the second electrode 61 of Figure 10 (paragraph 0059], wherein the electrodes are circular [i.e., rings]; paragraph 0128);

a nanopore adjacent to the first ring electrode and the second ring electrode and positioned to allow the chemical moiety to be positions in the first ring electrode and the second ring electrode (i.e., hole 12 of Figure 10; paragraph 0059); and

a voltage source for electrically connecting the first ring electrode to the second ring electrode for applying a ramping potential from the first ring electrode, through a portion of the chemical moiety in the nanopore to a second ring electrode to produce a signal indicative of a portion of the chemical moiety

(e.g., the electrodes measure ion transport across the hole [paragraph 0341], wherein a feedback capacitor ramps a voltage [paragraph 0345], and the electrical measurements are detected; paragraph 0342).

While Wang et al teach the apparatus comprises protein probes (e.g., a proteomics unit comprising antigen-antibody reactions; paragraph 0411), Wang et al do not specifically teach an array of protein probe molecules.

However, Chin et al teach a protein array (e.g., a solid support comprising multiple immobilized proteins; Abstract) having the added advantage of revealing disease mechanisms (column 3, lines 4-22).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the apparatus as taught by Wang et al with the array comprising protein probe molecules as taught by Chin et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in revealing disease mechanisms as explicitly taught by Chin et al (column 3, lines 4-22).

Regarding claim 16, the method of claim 1 is discussed above. Wang et al are silent with respect to the number of features on the array.

However, Chin et al teach an array (e.g., a solid support comprising multiple immobilized proteins; Abstract) comprising more that 100 features (e.g., 100 to 10,000 different kinds of antibodies; column 10, lines 25-30) with the added advantage that large numbers of antibodies (i.e., features) allow the study of a wide variety of protein in a single experiment (column 2, line 67-column 3, line 3).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the apparatus as taught by Wang et al with the array comprising more that 100 features as taught by Chin et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in allowing the study of a wide variety of protein in a single experiment as explicitly taught by Chin et al (column 2, line 67-column 3, line 3).

3. Claims 1, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (U.S. Patent Application Publication No. US 2002/0182627 A1, published 5 December 2002) in view of Denong Wang (PCT International Publication No. WO 02/083918A2, published 24 October 2002) as evidenced by Wade (Organic Chemistry, 2nd ed., Prentice-Hall, Englewood Cliffs, NJ (1997), page 1045).

Regarding claims 11 and 12, Wang et al teach the apparatus of claim 1 for identifying a chemical moiety from a sample solution, comprising:

a substrate having a channel (e.g., a microfluidic device having a channel; paragraphs 0062 and 0408 and Figures 13 and 21) with at least one array for capturing and releasing a chemical moiety from a sample solution (e.g., a proteomics unit or genomics unit; paragraphs 0411-412); and

a solid state nanopore system downstream from the substrate (Figure 21, wherein the first chamber is a proteomics or genomics unit [i.e., any appropriate test takes place in the first chamber], and the sample is transported from the first chamber to an ion transport detection unit; paragraph 0408) for identifying the chemical moiety received from the substrate channels after the chemical moiety has been released from the array (e.g., the ion transport detection unit receives the samples from the first chamber; paragraph 0408 and Figure 21), the nanopore system comprising:

a first ring electrode (e.g., a spiral electrode structure [paragraph 0038 and Figure 3B], wherein the electrodes are circular; paragraph 0128);

a second ring adjacent to the first ring electrode (e.g., the second electrode 61 of Figure 10 (paragraph 0059], wherein the electrodes are circular [i.e., rings]; paragraph 0128);

a nanopore adjacent to the first ring electrode and the second ring electrode and positioned to allow the chemical moiety to be positions in the first ring electrode and the second ring electrode (i.e., hole 12 of Figure 10; paragraph 0059); and

a voltage source for electrically connecting the first ring electrode to the second ring electrode for applying a ramping potential from the first ring electrode, through a portion of the chemical moiety in the nanopore to a second ring electrode to produce a signal indicative of a portion of the chemical moiety

(e.g., the electrodes measure ion transport across the hole [paragraph 0341], wherein a feedback capacitor ramps a voltage [paragraph 0345], and the electrical measurements are detected; paragraph 0342).

While Wang et al teach the apparatus comprises probes (e.g., a proteomics unit comprising antigen-antibody reactions; paragraph 0411), Wang et al do not specifically teach an array of carbohydrate or polysaccharide probe molecules.

Wade et al define polysaccharides as carbohydrates (page 1045, line 1); therefore, a polysaccharide probe is also a carbohydrate probe.

However, Denong Wang teaches an array of purified polysaccharides (i.e., polysaccharide probes) having the added advantage that purified polysaccharides are stable in various conditions and do not denature or undergo conformational alteration (page 73, line 30–page 74, line 4).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the apparatus as taught by Wang et al with the array comprising polysaccharide probes as taught by Denong Wang with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in probes that are stabile to various conditions and do not denature or undergo conformational alteration as explicitly taught by Denong Wang (page 73, line 30–page 74, line 4).

4. Claims 37-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (U.S. Patent Application Publication No. US 2002/0182627 A1, published 5 December 2002) in view of Ootsubo et al ((U.S. Patent Application Publication No. US 2003/0087297 A1, published 8 May 2003).

Regarding claim 37, Wang et al teach an apparatus for identifying a chemical moiety from a sample solution, comprising:

a substrate having a channel (e.g., a microfluidic device having a channel; paragraphs 0062 and 0408 and Figures 13 and 21) with at least one array for capturing a chemical moiety from a sample solution (e.g., a proteomics unit or genomics unit; paragraphs 0411-412); and

a solid state nanopore system downstream from the substrate (Figure 21, wherein the first chamber is a proteomics or genomics unit [i.e., any appropriate test takes place in the first chamber], and the sample is transported from the first chamber to an ion transport detection unit; paragraph 0408) for identifying the chemical moiety received from the substrate channels after the chemical moiety has been released from the array (e.g., the ion transport detection unit receives the samples from the first chamber; paragraph 0408 and Figure 21), the nanopore system comprising:

a first electrode layer having a first portion of the nanopore extending there through (e.g., a spiral electrode structure surrounding a hole in the substrate [paragraph 0038 and Figure 3B], wherein the electrodes are circular [paragraph 0128] and the hole is a funnel; Figure 2E and paragraph 0035) an exposing an electrode edge (e.g., the electrode edges are accessible to particles; paragraph 0273);

a first layer adjacent the first electrode layer (e.g., the substrate is multilayered; paragraph 0186), the first layer having a second portion of the nanopore there through, the first layer edge overhanging the first electrode edge (e.g., the hole extends through the layers of the substrate and is a funnel; Figure 2E and paragraph 0035);

a second electrode layer adjacent the to the first layer, the second electrode layer having a third portion of the nanopore there through (e.g., the first electrode 60 of Figure 2E [paragraph 0035], wherein the hole extends through the layers and is a funnel [Figure 2E and paragraph 0035] wherein the electrodes are circular [i.e., rings; paragraph 0128] and surround the bottom of the hole in the substrate [Figure 2E], thereby defining the nanopore) and defining a second electrode edge (e.g., the electrode edges are accessible to particles; paragraph 0273) the second electrode edge overhanging the first layer edge (e.g., the hole extends through the layers of the substrate and is a funnel; Figure 2E and paragraph 0035);

wherein the first electrode and the second electrode may be electrically ramped for sensing the chemical moiety (e.g., the electrodes measure ion transport across the hole [paragraph 0341], wherein a

feedback capacitor ramps a voltage [paragraph 0345], and the electrical measurements are detected; paragraph 0342).

While Wang et al teach a multilayered substrate (paragraph 0186) and also teach the use of insulating materials (paragraphs 0129 and 0396), Wang et al are silent with respect to an insulating layer between the electrodes.

However, Ootsubo et al teach an apparatus (e.g., a biochip; paragraph 0016) having a thin transparent layer of insulation between electrodes with the added advantage that the insulation layer allows the distance between the electrodes to be easily shortened, thereby achieving miniaturization and high speed (paragraph 0042).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the apparatus comprising layers between electrodes as taught by Wang et al with the insulation layer between the electrodes as taught by Ootsubo et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in allowing the distance between the electrodes to be easily shortened, thereby achieving miniaturization and high speed as explicitly taught by Ootsubo et al (paragraph 0042).

Regarding claim 38, the nanopore structure of claim 37 is discussed above. Wang et al also teach a substrate adjacent to the first electrode (e.g., the electrodes are provided on separate layers [paragraph 0186], wherein each layer is interpreted as a substrate for these additional structures).

Regarding claim 39, the nanopore structure of claim 37 is discussed above. Wang et al also teaches the first electrode edge defines a diameter that is smaller than the second diameter portion that is defined by the first layer edge (e.g., the hole extends through the layers of the substrate and is a funnel; Figure 2E and paragraph 0035).

Regarding claim 40, the nanopore structure of claim 37 is discussed above. Wang et al also teaches a second layer contacting the second electrode layer and being adjacent to the nanopore (e.g., the

substrate is multilayered; paragraph 0186), the second layer having a fourth portion of the nanopore there through and defining a second edge, the second edge overhanging the second electrode edge (e.g., the hole extends through the layers of the substrate and is a funnel; Figure 2E and paragraph 0035).

Regarding claim 41, the nanopore structure of claim 37 is discussed above. Wang et al also teach the second edge defines a third diameter portion that is smaller than the second diameter portion of the nanopore (e.g., the hole extends through the layers of the substrate and is a funnel; Figure 2E and paragraph 0035).

Regarding claims 42-44, the nanopore structure of claim 40 is discussed above. Wang et al also teach the first electrode layer and the second electrode layers comprise ring structures (e.g. the electrodes are circular [i.e., rings]; paragraph 0128).

Regarding claim 45, the nanopore structure of claim 40 is discussed above. Wang et al also teach electric circuits (paragraph 0058).

Regarding claim 46, the nanopore structure of claim 37 is discussed above. Wang et al also teach the electric circuit further comprises a voltage source for electrically connecting the first electrode layer with the second electrode layer and generating a potential between the first electrode layer and the second layer for sensing a chemical moiety in the nanopore (e.g., the electrodes measure ion transport across the hole [paragraph 0341], wherein a feedback capacitor ramps a voltage [paragraph 0345], and the electrical measurements are detected; paragraph 0342).

Regarding claim 47, the nanopore structure of claim 37 is discussed above. Wang et al also teach the voltage source comprises a time varying voltage source (e.g., the voltage ramps with time; paragraph 0345).

Regarding claim 48, the nanopore structure of claim 40 is discussed above. Wang et al also teach a current sensor for sensing a resulting current (e.g., a device for recording current; paragraph 0342).

Regarding claims 49 and 50, the nanopore structure of claim 37 is discussed above. Wang et al also teach the electrode layers are gold (paragraph 0128).

Regarding claim 51, the nanopore structure of claim 40 is discussed above. Wang et al also teach the pores are form 1 nanometer to 300 nanometers (e.g., about .1 micrometers; paragraph 337).

5. Claims 52-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (U.S. Patent Application Publication No. US 2002/0182627 A1, published 5 December 2002) and Ootsubo et al ((U.S. Patent Application Publication No. US 2003/0087297 A1, published 8 May 2003) as applied to claim 40 above, and further in view of Peters (U.S. Patent No. 4,543,271, issued 24 September 1985).

Regarding claims 52-53, the structure of claim 40 is discussed above. Neither Wang et al or Ootsubo et al teach materials for the insulator layers.

However, Peters teaches the use of silicon dioxide as an insulating layer with the added advantage that a layer of silicon dioxide prevents long-term air oxidation (column 8, lines 57-60).

It would therefore have been obvious to modify the structure as taught by Wang et al and Ootsubo et al with silicon dioxide as taught by Peters with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in preventing long term air oxidation as explicitly taught by Peters (column 8, lines 57-60).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1-6, 15, 30, 32-35, 37-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 10/352,675. Both sets of claims are drawn to first and second electrodes, ring electrodes, ramping potentials, nanopores between the electrodes, substrates for positioning the electrodes, signal detection means, and charged polymers (i.e., nucleic acids). The open claim language "comprising" in the instant claims encompasses the additional limitation of short ramp times found in the '675 claims.

This is a provisional obviousness-type double patenting rejection.

2. Claims 1-20 and 30-53 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 10/631,033 in view of Wang et al (U.S. Patent Application Publication No. US 2002/0182627 A1, published 5 December, 2002). Both sets of claims are drawn to substrates, having channels, nanopore systems, array, nucleic acids, carbohydrates, silicon, and proteins. The claims of the '033 application do not have the electrodes of the instant claims.

However, Wang et al teach an apparatus for identifying a chemical moiety from a sample solution, comprising:

a substrate having a channel (e.g., a microfluidic device having a channel; paragraphs 0062 and 0408 and Figures 13 and 21) with at least one array for capturing a chemical moiety from a sample solution (e.g., a proteomics unit or genomics unit; paragraphs 0411-412); and

a solid state nanopore system downstream from the substrate (Figure 21, wherein the first chamber is a proteomics or genomics unit [i.e., any appropriate test takes place in the first chamber], and the sample is transported from the first chamber to an ion transport detection unit; paragraph 0408) for identifying the chemical moiety received from the substrate channels after the chemical moiety has been released from the array (e.g., the ion transport detection unit receives the samples from the first chamber; paragraph 0408 and Figure 21), the nanopore system comprising:

electrodes (e.g., a spiral electrode structure surrounding a hole in the substrate [paragraph 0038 and Figure 3B], wherein the electrodes are circular [paragraph 0128] and the hole is a funnel; Figure 2E and paragraph 0035) an exposing an electrode edge (e.g., the electrode edges are accessible to particles; paragraph 0273) with the added advantage that electrodes allow measurement of ion transport across the holes (paragraph 0341).

It would therefore have been obvious to modify the instant claims with the short ramp times as taught by Wang et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in allowing measurement of ion transport across the holes as explicitly taught by Wang et al (paragraph 0341).

This is a provisional obviousness-type double patenting rejection.

3. Claims 1-20 and 30-53 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4-15 of copending Application No. 10/898,586. Both sets of claims are drawn to substrates, nanopores, ramping potentials ring electrodes, and polynucleotides. The open claim language "comprising" in the instant claims encompasses the quenchable and excitable moieties of the '586 claims.

This is a provisional obviousness-type double patenting rejection.

Conclusion

1. No claim is allowed.

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert T. Crow
Examiner
Art Unit 1634

BJ FORMAN, PH.D.
PRIMARY EXAMINER